Remarks

Claims 17-30 were pending before entry of the present amendment. Claims 17-24, and 26-30 have been canceled without prejudice to pursuing the claimed subject matter in other applications. Claim 25 has been amended to more particularly point out and distinctly claim the subject matter of the instant invention. New claims 31-46 have been added. The amended and new claims are supported by the specification as originally filed as follows:

Claim	Examples of support
25, 31, 32, 41	Example 1, pages 30-31
33	Example 3, page 32
34, 35, 36, 37, 38, 39, 40	Example 1, pages 30-31; page 14, line 30 to page 15, line 18; page 26, lines 10-13
42	Page 14, line 30 to page 15, line 18; page 26, lines 10-13
43-44	Page 29, lines 24-28
46	Page 29 , lines 29-31

Thus, no new matter has been introduced and after entry of the present amendment, claims 25 and 31 to 46 will be pending in the instant application.

Priority

In order to ensure that the present application properly contains a specific reference to the earlier filed application, an amendment to the specification is set forth on page 2 of the present Amendment, so that the first sentence of the specification claims benefit of U.S. Application Serial No. 09/531,375 filed March 21, 2000, now U.S. Patent No. 6,764,685 B1, issued July 20, 2004. This reference now contains the updated status of the earlier filed application.

The Claim Rejections under 35 U.S.C. § 112, Second Paragraph, Should be Withdrawn

Claims 17-30 were rejected under 35 U.S.C. § 112, second paragraph, as being allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicants regard as the invention. In particular, the Examiner contends that the intended chimeric virus as claimed is not well defined. Further, the Examiner contends that for something to be chimeric it has to encompass distinct elements both of which have to be defined by their respective limitations.

Applicants have canceled claims 17-24 and 26-31, amended claim 25 and submit new claims in order to more distinctly point out the elements which constitute the recombinant viruses administered in the methods of the invention. In particular, amended claim 25 and new claim 36 recite that the recombinant virus has a Kansas-strain bovine parainfluenza virus type 3 (PIV3) backbone and recites specific nucleotide sequences in the backbone at which heterologous sequences may be added. New claim 33 recites that the parainfluenza virus comprises nucleotide sequences of a Kansas-strain bovine PIV3 genome and sequences of human PIV3. New claims 32, 34, 35 and 37 recite that the virus comprises particular nucleotides of the genome of Kansas strain PIV3 and nucleotide sequences of another virus. Thus, both the virus backbone and the heterologous sequences of the recombinant viruses recited in the amended and new claims have been adequately defined and the rejection of the claims for allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicants regard as the invention should be withdrawn.

The other claims rejections under 35 U.S.C. § 112, second paragraph, for being allegedly incomplete for omitting essential elements, vague and indefinite for not defining the heterologous sequences, indefinite for the recitation of "mutations or modifications", and improper multiple dependent form are moot in view of the present claim amendments and the rejections should be withdrawn.

The Claim Rejections under 35 U.S.C. § 112, First Paragraph, Should be Withdrawn

Claims 17-30 are rejected under 35 U.S.C. §112, first paragraph, for alleged failure of the specification to provide enablement for the full scope of the claims. While the rejections of claims 17-24 and 26-30 are moot in view of the present claim amendments, applicants respectfully submit that, for the reasons discussed below and according to the applicable case law, the instant specification does fully enable one of skill in the art to make and use viruses corresponding to the scope of the presently pending claims.

THE LEGAL STANDARD

The test for enablement is whether one reasonably skilled in the art could make or use the invention, without undue experimentation, from the disclosure in the patent specification coupled with information known in the art at the time the patent application was filed. *U.S. v. Telectronics Inc.*, 857 F.2d 778, 8 USPQ2d 1217 (Fed. Cir. 1988). In fact, well known subject matter is preferably omitted. *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384 (Fed. Cir. 1986) ("a patent need not teach, and preferably omits, what is well know in the art."). Further, one skilled in the art is presumed to use the information available to him in attempting to make or use the claimed invention. *See Northern Telecom, Inc. v. Datapoint Corp.*, 908 F.2d 931, 941 (Fed. Cir. 1990) ("A decision on the issue of enablement

requires determination of whether a person skilled in the pertinent art, using the knowledge available to such a person and the disclosure in the patent document, could make and use the invention without undue experimentation."). These enablement rules preclude the need for the patent applicant to "set forth every minute detail regarding the invention." *Phillips Petroleum Co. v. United States Steel Corp.*, 673 F. Supp. 1278, 1291 (D. Del. 1991); *see also DeGeorge v. Bernier*, 768 F.2d 1318, 1323 (Fed. Cir. 1985).

Undue experimentation is experimentation that would require a level of ingenuity beyond what is expected from one of ordinary skill in the field. *Fields v. Conover,* 170 USPQ 276, 279 (CCPA 1971). The factors that can be considered in determining whether an amount of experimentation is undue have been listed in *In re Wands,* 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Among these factors are: the amount of effort involved, the guidance provided by the specification, the presence of working examples, the amount of pertinent literature and the level of skill in the art. The test for undue experimentation is not merely quantitative, since a considerable amount of experimentation is permissible, so long as it is merely routine. *Id.*

Further, while the predictability of the art can be considered in determining whether an amount of experimentation is undue, mere unpredictability of the result of an experiment is not a consideration. Indeed, the Court of Custom and Patent Appeals has specifically cautioned that the unpredictability of the result of an experiment is not a basis to conclude that the amount of experimentation is undue in *In re Angstadt,* 190 USPQ 214 (CCPA 1976):

> [If to fulfill the requirements of 112, first paragraph, an applicant's] disclosure must provide guidance which will enable one skilled in the art to determine, with reasonable certainty before performing the reaction whether the claimed product will be obtained, . . . then all "experimentation" is "undue" since the term "experimentation" implies that the success of the particular activity is uncertain. Such a proposition is contrary to the basic policy of the Patent Act.

Id. at 219 (emphasis in the original).

THE INSTANT SPECIFICATION PROVIDES AMPLE GUIDANCE TO THE SKILLED ARTISAN FOR MAKING THE CLAIMED VIRUSES FOR USE WITH THE CLAIMED METHODS

The claimed invention relates to methods of administering to a subject a recombinant parainfluenza virus comprising nucleotide sequences of a Kansas-strain bovine parainfluenza virus type 3 genome and one or more heterologous sequences. The instant application provides all the information required by one of skill in the art to construct and generate a recombinant virus with one or more heterologous sequences.

As indicated, the specification as filed provides ample guidance for how to make the recombinant viruses of the claimed invention. For example, the specification as filed

describes approaches for how to construct the recombinant virus (*see, e.g.,* page 18, line 13 to page 21, line 5). The instant specification teaches that the heterologous gene sequences can be derived from any number of sequences, including but not limited to several viruses, including but not limited to, RSV, PIV, New Castle Disease virus, Sendai virus, Infectious Laryngotracheitis virus, or influenza (*see, e.g.,* the specification at page 14, line 30 to page 15, line 18). It is also taught how to construct and clone a recombinant parainfluenza virus comprising nucleotide sequences of Kansas-strain bovine parainfluenza virus type 3 (bPIV3) and heterologous sequences consisting of the F and HN gene sequences of human parainfluenza virus type 3 (hPIV3) (*see, e.g.,* the specification at Example 1, on pages 30 to 31). In particular, the instant specification discloses how to introduce a restriction enzyme site at specific nucleotide positions of the bPIV3 cDNA, particularly nucleotide positions 5041 and 8529 (*see, e.g.,* the specification at page 30, lines 10 to 14). The instant specification further teaches how to isolate the hPIV3 F and HN nucleotide sequences using recombinant DNA techniques (*see, e.g.,* the specification at page 30, line 15 to page 31, line 5). It is also taught how to construct the full length bPIV3/hPIV3 cDNA by ligating the bPIV3 sequences to the hPIV3 F and HN sequences (*see, e.g.,* the specification at page 31, lines 6 to 12 of the specification as filed). Further, Applicants respectfully point out that the skill in the field of molecular biology is very high. Thus the skilled artisan would have been able at the time of filing of the application to generate the claimed recombinant viruses.

Preparation of the recombinant viruses is also taught in the specification as filed (*see, e.g.,* the specification at page 22, line 16 to page 25, line 27). For example, the instant specification teaches how to prepare the bPIV3/hPIV3 via rescue of the virus in either Hela or Vero cells (*see, e.g.,* the specification at Example 2, on page 31). Furthermore, the specification as filed teaches that RT-PCR can be employed in order to confirm that the rescued virus is the bPIV3/hPIV3 (*see, e.g.,* the specification at Example 3, on page 32). In particular, the instant specification teaches PCR amplification of nucleotide 5,255 to 6,255 of the recombinant parainfluenza virus resulting in a DNA fragment that is recognized by restriction endonucleases Sac 1 and Bg1 II, confirming that the isolated sequences are from hPIV3 (*see, e.g.,* the specification at page 32, lines 10 to 15). The instant specification further teaches PCR amplification of nucleotide 9,075 to 10,469 of the parainfluenza virus resulting in a DNA fragment that is recognized by restriction endonucleases PvuII and Bam H1, confirming that the isolated sequences are from bPIV3 (*see, e.g.,* the specification at page 32, lines 15 to 20).

With regard to how to use the invention, the application as originally filed describes how to use the recombinant viruses of the invention in a variety of different ways (*see, e.g.,* the specification at page 21, line 28 to page 22, line 14 and from page 26, line 1 to page 30, line 2). For example, the specification describes how to use the recombinant viruses to

express the gene products encoded by the heterologous sequences (*see, e.g.,* the specification at section 5.2, page 21, line 28 to page 22, line 14). The specification as filed also describes how to use the recombinant viruses of the invention as immunogenic compounds and as vaccines (*see, e.g.,* the specification at page 26, line 1 to page 30, line 2).

The instant specification discloses administration of the claimed viruses in a subject via oral, intradermal, intramuscular, intrapertioneal, intravenous, subcutaneous, and intranasal routes (*see, e.g.,* the specification at page 29, lines 29 to 31). The specification clearly teaches that recombinant viruses of the invention can be administered in a subject in order to elicit an immune response (*see, e.g.,* the specification at Example 4, pages 32-24). For example, the instant specification describes the strong protective response that was elicited in an animal model immunized with the recombinant parainfluenza virus comprising nucleotide sequences of Kansas-strain bovine parainfluenza virus type 3 (bPIV3) and heterologous sequences consisting of the F and HN gene sequences of human parainfluenza virus type 3 (hPIV3) heterologous sequences (*see, e.g.,* the specification at Table 2, page 34; page 33, lines 27-30). In particular, the instant specification shows the antibody response generated in the hamsters upon being infected with the different PIV3 strains and shows that the serum titers for hamsters infected with the recombinant bPIV3/hPIV3 virus was equivalent to those infected with wild type hPIV3 (*see, e.g.,* the specification at Table 2, page 34). The specification as originally filed further teaches that the claimed viruses may be formulated with a suitable adjuvant in order to enhance the immunological response (*see, e.g.,* the specification at page 29, lines 24 to 28).

Thus, Applicants submit that the specification, coupled with the state of the art as of the effective filing date of the instant application, fully enables one of skill in the art to make, use, and practice the invention as claimed without undue experimentation. Applicants respectfully request that the rejections under 35 U.S.C. § 112, first paragraph, be withdrawn.

The Claim Rejections under 35 U.S.C. § 112, First Paragraph, Should be Withdrawn

Claims 17-30 are rejected under 35 U.S.C. §112, first paragraph, for allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention. In particular, the Examiner contends that the Applicants are not in possession of the broad scope of the claimed product and thus not in possession of the method of using the product. While the rejection of claims 17-24 and 26-30 are moot in view of the present claim amendments, Applicants respectfully submit that the currently pending claims contain subject matter that is described in the specification in such a way to convey to one skilled in the art that the inventors, at the time the application was filed, had possession of the claimed invention.

The pending claims relate to a method of administering to a subject a recombinant parainfluenza virus comprising nucleotide sequences of a Kansas-strain bovine parainfluenza virus type 3 genome (bPIV3) and one or more heterologous sequences. The specification as filed provides a sufficient written description to convey that the inventors were in possession of the claimed invention. Possession of the claimed invention may be shown in a variety of ways including description of an actual reduction to practice, which can be shown by describing testing of the claimed invention. *See, e.g., M.P.E.P.* 2163 I. The application provides such written description support. For example, the working examples show how to construct and clone a recombinant parainfluenza virus of the invention, a Kansas-strain bPIV3 with heterologous sequences consisting of the F and HN gene sequences of hPIV3, using recombinant DNA technology (*see, e.g.,* the specification at Example 1, p. 30). The working examples also provide a description of the protocols and assays that can be used for the rescue and confirmation of the recombinant viruses of the invention (*see, e.g.,* the specification at Example 2, on page 31 and Example 3, on page 32). The specification further provides ample disclosure to allow one of skill in the art to assay the claimed viruses to ensure that they are attenuated and capable of eliciting an immune response (*see, e.g.*, the specification at Example 4, pages 32-34). For example, the specification provides biochemical and/or immunochemical based assays, such as the $TCID_{50}$ assay, to determine the growth rate of the recombinant constructs of the invention to assess their viability in *in vivo* systems (*see, e.g.*, the specification at Example 4, pages 32-33). The instant specification further provides a description of the assays used to demonstrate that when an animal model is infected with a recombinant virus of the invention, a strong antibody response is generated (*see, e.g.*, the specification at Example 4, pages 33-34). Thus, the specification provides an adequate written description, through the working examples, to demonstrate to one skilled in the art that the inventors were in possession of the claimed methods.

Furthermore, the state of the art of molecular biology and virology was fairly advanced at the time the application was filed. Therefore, the working examples in the specification, the considerable direction and guidance on how to practice the claimed invention and the high level of skill in the art evidence that applicants were in possession of the claimed invention.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention. *See, e.g., M.P.E.P.* 2163 I. citing to *Moba, B.V. v. Diamond Automation Inc.,* 325 F.3d 1306, 1319, 66 USPQ2d 1429, 1438 (Fed. Cir. 2003); *Vas-Cath, Inc. v. Mahurkar,* 935 F.2d at 1563, 19 USPQ2d at 1116. Furthermore, what is conventional or well known to one of skill in the art need not be disclosed in detail

and, where the level of knowledge and skill in the art is high, a written description question should not be raised. *See, e.g., Capon v. Eshhar*, 418 F.3d 1349, at 1357 (Fed. Cir. 2005).

Applicants submit that the instant specification coupled with the information which was readily available to the skilled artisan at the time the instant application was filed is sufficient to satisfy the written description requirement. Thus, Applicants respectfully request that the Examiner withdraw the rejection under 35 U.S.C. § 112, first paragraph.

The Obviousness Type Provisional Double Patenting Rejection of the Claims Should be Held in Abeyance Until Indication of Allowable Subject Matter

Claims 17-30 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 38-50 of copending Application No. 10/934,864 ("the '864 application").

Without acquiescing to the Examiner's rejection, Applicant points out that according to MPEP §804(I)(B), if the provisional double patenting rejections in both applications are the only rejections remaining in those applications, the Examiner should then withdraw that rejection in one of the applications and permit the application to issue as a patent.

Therefore, Applicant respectfully requests that if the Examiner maintains the present rejection, the Examiner hold this provisional double-patenting rejection in abeyance until such time as relevant claims of the '864 application or the instant application, are allowable.

The Claim Rejections under 35 U.S.C. § 102 Should be Withdrawn

Claims 17-24 and 30 were rejected under 35 U.S.C. § 102(b) as being allegedly anticipated by Murphy *et al.* (WO 98/53078) and claims 17-24 were rejected under 35 U.S.C. § 102(e) as being allegedly anticipated by Schmidt *et al.* (WO 01/04320). Applicants respectfully disagree with the rejections. However, in view of the present claim amendments, the rejections are moot and should be withdrawn.

CONCLUSION

Applicants respectfully request that the above amendments be entered and made of record in the present application file.

Respectfully submitted,

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